Decision Summary

CMS received a request to delete the national noncoverage of blood flow measurement from the Magnetic Resonance Imaging NCD at 220.2 of the NCD Manual and thus permit local Medicare contractor discretion to cover this use under 220.2(D). The requestor points to an apparent contradiction between this noncoverage provision and the national coverage of magnetic resonance imaging under the Magnetic Resonance Angiography NCD at 220.3 of the NCD Manual.

CMS also received a separate request to revise the reference to cardiac pacemakers to permit coverage for MRI when a beneficiary has an implanted device that has been designed, tested and FDA labeled for use in the MRI environment. NCD 220.2 currently includes the following:

The MRI is not covered when the following patient-specific contraindications are present. It is not covered for patients with cardiac pacemakers or with metallic clips on vascular aneurysms.

We have considered both requests in this reconsideration.

CMS finds that the blanket noncoverage of MRI for blood flow determination at 220.2 is no longer supported by the available evidence. Therefore we will remove the phrase "blood flow measurement," from the Nationally Noncovered Indications at 220.2(C)(2) of the National Coverage Determinations Manual. Pursuant to 220.2(D), local Medicare contractors will have discretion to cover (or not cover) this use.

CMS has not found evidence that MRI improves health outcomes in beneficiaries who have an implanted cardioverter-defibrillator or cardiac pacemaker approved by FDA for use in an MRI environment. We also note that there are currently no such devices. Therefore we will not change this provision of the NCD Manual. We will retain the current contraindications.

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Decision Memo

TO: Administrative File: CAG # 00399R Magnetic Resonance Imaging

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SUBJECT: Final Decision Memorandum for CAG # 00399R Magnetic Resonance Imaging
DATE: September 28, 2009

I. Final Decision

CMS received a request to delete the national noncoverage of blood flow measurement from the Magnetic Resonance Imaging NCD at 220.2 of the NCD Manual and thus permit local Medicare contractor discretion to cover this use under 220.2(D). The requestor points to an apparent contradiction between this noncoverage provision and the national coverage of magnetic resonance imaging under the Magnetic Resonance Angiography NCD at 220.3 of the NCD Manual.

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CMS has not found evidence that MRI improves health outcomes in beneficiaries who have an implanted cardioverter-defibrillator or cardiac pacemaker approved by FDA for use in an MRI environment. We also note that there are currently no such devices. Therefore we will not change this provision of the NCD Manual. We will retain the current contraindications.

II. Background

Magnetic resonance imaging (MRI, formerly known as nuclear magnetic resonance imaging - NMRI) is a noninvasive method of graphically representing the distribution of water and other hydrogen-rich molecules in the human body. Magnetic resonance imaging is a diagnostic imaging modality that is capable of demonstrating a wide variety of soft-tissue lesions with contrast resolution equal or superior to CT scanning in various parts of the body. Among the advantages of MRI are the absence of ionizing radiation and the ability to achieve high levels of tissue contrast resolution without injected iodinated radiological contrast agents. The terms CMR and CMRI refer respectively to cardiac magnetic resonance and cardiac MRI.

We provide a very simplified discussion below for the lay reader. Systole describes the period during which the right and left cardiac ventricles contract forcefully and eject blood into the pulmonary artery and the aorta respectively. Diastole describes the period during which the relaxed ventricles fill with blood. There are four cardiac valves in the normal human heart. During diastole blood in the right atrium flows through the tricuspid valve into the right ventricle and blood in the left atrium flows through the mitral valve into the left ventricle. During systole blood in the right ventricle flows through the pulmonic valve into the pulmonary artery and blood in the left ventricle flows through the aortic valve into the aorta.

The following terms refer to abnormal function of cardiac valves: AS = aortic stenosis; AR = aortic regurgitation; MS = mitral stenosis; MR = mitral regurgitation. Stenosis indicates a narrowing of the valve opening and regurgitation indicates backflow of blood through a valve that fails to close completely. Either condition may lead to deterioration of cardiac function. Valvular dysfunction may arise from a variety of causes such as heritable conditions, infections, rheumatic disease, ischemia and degenerative calcification.

Many diagnostic modalities may contribute to a diagnosis of valvular disease. Physical examination, electrocardiography (EKG), echocardiography, plain X-rays or more complex imaging, and catheterization have been used. Valvular abnormalities may be visualized directly, i.e. by the identification of abnormal anatomic structure or a reduced cross sectional area of the valve's opening, or indirectly via measurement of the speed (velocity) and volume of blood flow through the opening. Medical and/or surgical treatments may be recommended depending on the underlying cause and the severity of the dysfunction. A detailed discussion of the pathophysiology and treatment of specific valvular conditions is beyond the scope of this memorandum.

Magnetic resonance imaging exposes the patient to strong magnetic fields which may cause the movement or heating of implanted medical devices that are ferromagnetic (e.g. surgical clips) or that have ferromagnetic components (e.g. pacemakers, prostheses.) Such movement can have catastrophic effects on the patient. The American College of Radiology's ACR Guidance Document for Safe MR Practices: 2007 explicitly speaks to the need to address the possibility that the patient may have ferromagnetic foreign bodies or implants.

III. History of Medicare Coverage

Section 220.2 of the NCD Manual speaks to coverage of MRI. CMS originally set forth the conditions under which MRI may be covered in November, 1985. Revisions to the policy took place in 1988, 1991, and 1994 to provide coverage for additional conditions. Currently covered indications include using MRI to examine the head, central nervous system, and spine. MRI can also assist in the differential diagnosis of mediastinal and retroperitoneal masses, including abnormalities of the large vessels such as aneurysms and dissection. MRI may also be used to detect and stage pelvic and retroperitoneal neoplasms and to evaluate disorders of cancellous bone and soft tissues. The MRI may also be covered to diagnose disc disease without regard to whether radiological imaging has been tried first to diagnose the problem. Blood flow measurement, imaging of cortical bone and calcifications, and procedures involving spatial resolution of bone and calcifications, are nationally non-covered indications. All other uses of MRI for which CMS has not specifically indicated are under local contractor discretion. The MRI is not covered when patient-specific contraindications such as cardiac pacemakers, metal clips on vascular aneurysms, viable pregnancy, acutely ill patients requiring life support systems and monitoring devices that employ ferromagnetic materials, or patients suffering from claustrophobia, are present.

We note for the readers' convenience that some uses of MRI related to blood flow are specifically determined in the Magnetic Resonance Angiography NCD at 220.3 of the NCD Manual.

A. Current Request

The requestors have asked CMS to reconsider Section 220.2 to remove the reference to blood flow measurement in the nationally non-covered indications.

During the initial 30-day comment period, CMS received a request from Medtronic, Inc. to modify the Contraindications section to permit coverage of MRI when the beneficiary has an implanted device such as a cardiac pacemaker that has been designed, tested and FDA labeled for use in the MRI environment.

B. Benefit Category

Medicare is a defined benefit program. An item or service must fall within a benefit category as a prerequisite to Medicare coverage §1812 (Scope of Part A); §1832 (Scope of Part B) and §1861(s) (Definition of Medical and Other Health Services) of the Act. Magnetic resonance imaging is considered to be within the following benefit category: other diagnostic tests §1861(s)(3). This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem." Thus, except where other uses have been explicitly authorized by statute, Medicare does not cover diagnostic testing used for routine screening or surveillance.

IV. Timeline of Recent Activities

January 20, 2009	CMS opens this reconsideration of the NCD on Magnetic Resonance Imaging (MRI).
February 19, 2009	The initial 30 day public comment period ended. Eighty-six comments were received.
March 16, 2009	During the initial 30-day comment period, CMS received a request from Medtronic, Inc. to modify the Contraindications section to permit coverage of MRI when devices such as cardiac pacemakers have been designed, tested and FDA labeled for use in the MRI environment. CMS solicits additional public comment for 30 days on this aspect of the request. Six comments were received.
June 30, 2009	Proposed decision posted
July 30, 2009	The 30-day public comment period ended. Eight comments were received.

V. FDA Status

The Food and Drug Administration (FDA) has approved or cleared magnetic resonance diagnostic devices from various manufacturers. A detailed enumeration of those devices is beyond the scope of this memorandum. At this time, FDA has not approved any implantable cardioverter-defibrillators or pacemakers for use in an MRI environment.

VI. General Methodological Principles

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for beneficiaries. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the Agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A.

Public commenters sometimes cite the published clinical evidence and provide CMS with useful information. Public comments that provide information based on unpublished evidence, such as the results of individual practitioners or patients, are less rigorous and, therefore, less useful for making a coverage determination. CMS uses the initial comment period to inform the public of its proposed decision. CMS responds in detail to the public comments that were received in response to the proposed decision when it issues the final decision memorandum.

VII. Evidence

A. Introduction

Below is a summary of the evidence we considered during our review.

The Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem."

The original requestors did not ask for national Medicare coverage of MRI for the assessment of blood flow, but specifically requested the removal of the national noncoverage provision so that Medicare contractors could determine coverage for MRI claims without this broad national noncoverage provision. The requestors submitted evidence relating to the use of MRI to determine cardiac blood flow to support their request for removal of the blanket national noncoverage provision regarding blood flow. Thus, we reviewed evidence demonstrating that the MRI assessment of cardiac blood flow can be used in the management of a Medicare beneficiary's medical problem and improves patient outcomes.

We did not review evidence that was focused on pediatric study populations, as it is not generalizeable to the Medicare beneficiary population. We did not review evidence that focused on technologic feasibility in normal subjects as these data do not speak to the outcomes attributable to the use of MRI for the management of disease. We did not find evidence suggesting any disparate effect of this technology on historically underserved populations. We have for the readers' reference included all of the requestors' submitted articles in Appendix B.

The secondary requestor (Medtronic) did not ask for national Medicare coverage of any particular use of MRI, but specifically requested the removal of the national noncoverage provision containing the contraindication related to implanted devices such as pacemakers. Thus, we looked for evidence demonstrating that MRI assessment in a beneficiary with an implanted pacemaker of cardioverter-defibrillator improves patient health outcomes.

B. Discussion of Evidence Reviewed

1. Questions

The original request

Q1. Is the evidence adequate to conclude that MRI assessment of cardiac blood flow informs the diagnosis of cardiac valvular, cardiac shunt, cardiac stroke and ejection volume pathologies, compared to diagnosis of these conditions without MRI assessment of cardiac blood flow?

Q2. Is the evidence adequate to conclude that the MRI assessment of cardiac blood flow improves health outcomes in patients who have valvular pathology, intracardiac shunts, stroke volume abnormalities or reduced ejection fraction?

The secondary request

Q3. Is the evidence adequate to conclude that MRI improves health outcomes in Medicare beneficiaries who have implanted devices such as pacemakers or implantable cardioverter-defibrillators that have been approved by FDA as safe for use in an MRI environment?

2. External Technology Assessments

CMS did not request an external technology assessment (TA) on this issue from the Agency for Healthcare Research and Quality (AHRQ).

3. Internal technology assessment

The original request

The reviewed evidence was gathered from articles submitted by the original requestor and a literature search of the PubMed database. CMS performed an extensive literature search utilizing PubMed for search terms involving MRI and cardiac blood flow. Summaries are provided below, organized by year in reverse chronologic order. Please see the evidence tables for additional details about the characteristics of the study subjects. The evidence included comparisons of MRI with other diagnostic technologies as well as studies where MRI was used to assess the results of alternative cardiac treatment strategies.

Tanaka et al. (2007)
The authors sought to assess whether velocity-encoded phase-contrast MRI can provide an alternate means of quantifying aortic valve area (AVA) by CMRI. Twenty-two consecutive AS patients were imaged with CMRI. AVA was determined by velocity-encoded phase contrast (VEPC) imaging and by direct planimetry. Mean AVA by planimetry was 1.05± 0.41 cm^2 and 1.00± 0.4 cm^2 by VEPC, with a strong correlation (R^2 = 0.86, $p < 0.0001$) between the two methods. The mean difference of AVA was 0.05± 0.15 (95% CI = [0.02-0.08]), and the limits of agreement were -0.26 to 0.36 cm^2. The mean difference between 2 observers for planimetry was 0.030± 0.07 (95% CI 0.02-0.04) with limits of agreement of -0.11 to 0.16 cm^2 and for VEPC was 0.008± 0.085 (95% CI -0.01-0.026) with limits of agreement of -0.16 to 0.18 cm^2. The authors concluded that VEPC CMRI is an alternative method to direct planimetry for accurately determining AVA.

Yap et al. (2007)
The authors aimed to compare velocity-encoded cine cardiac magnetic resonance (CMR) with an established echocardiographic method for noninvasive measurement of aortic valve area (AVA) using the continuity equation. Twenty consecutive young adults with stenotic bicuspid aortic valves were examined with CMR and transthoracic echocardiography (TTE). CMR AVA was calculated by the continuity equation, dividing stroke volume by the aortic velocity-time integral (VTIAorta), the stroke volume measured both by ventricular volume analysis and by phase contrast velocity mapping at 4 levels (1 subvalvar and 3 supravalvar). Stroke volumes measured at all levels correlated well with those from volumetric analysis. The CMR AVAs calculated using volumetric analysis and VTIAorta from jet velocity mapping correlated and agreed well with TTE AVA measurements (R^2 = 0.83). When CMR AVA was calculated more rapidly using volume flow and VTIAorta both measured from the same trans-jet velocity acquisition, R2 was 0.74, with a bias and limits of agreement of 0.02 (-0.44, 0.47) cm^2. The authors concluded that continuity equation calculation of the AVA using CMR velocity mapping, with or without ventricular volumetric measurement, correlated and agreed well with the comparable and widely accepted TTE approach.

Gelfand et al. (2006)
The investigators sought to define the CMR regurgitant fractions that best correlate with qualitative mild, moderate, and severe regurgitation by color Doppler echocardiography. Data from 141 consecutive patients (age 53 ± 15 yr; 43% female) with contemporary (median, 31 days) CMR and echocardiographic data, including 107 regurgitant valves and 70 normal valves, were compared. Thresholds were developed on an initial cohort of patients with 55 regurgitant valves, and subsequently tested on a later cohort of patients with 52 regurgitant valves. Regurgitation fraction (RF) limits that optimized concordance of CMR and echo severity grades were similar for MR (mitral regurgitation) and AR (aortic regurgitation) and were: mild ± 15%, moderate 16-25%, moderate-severe 26-48%, severe > 48%. The authors concluded that their study provided simple qualitative threshold grades for MR and AR severity that allows for standardized reporting of regurgitation severity by CMR and excellent correlation with clinical echocardiography.

Paelnick et al. (2005)
The aim of this study was to compare tissue magnetic resonance (MR) imaging with tissue Doppler imaging for the estimation of filling pressure, in comparison with invasive measurement. The authors state that transmitral flow is unreliable for the estimation of left ventricular (LV) filling pressures in hypertrophy and normal systolic function. They further state that normalizing early mitral velocity (E) for the influence of myocardial relaxation by combining E with early diastolic mitral septal tissue velocity (Ea) provides better Doppler estimates of filling pressures. The authors studied 18 persons with hypertensive heart disease (LV mass index: 114 ± 21 g/m^2), absence of valvular regurgitation, and with normal or mildly reduced systolic function (LV ejection fraction: 57.6 ± 6.5%) referred for cardiac catheterization. They all underwent consecutive measurement of mitral flow and septal tissue velocities with phase-contrast MR and Doppler. These data were compared with mean pulmonary capillary wedge pressure (PCWP). There was a strong relation between MR (11.6 ± 4.3) and Doppler-assessed (12.1 ± 3.5) E/Ea (95% confidence interval of -1.5 to 0.5) ($r = 0.89$, $p < 0.0001$). In addition, E/Ea related strongly to invasively measured PCWP (MR: $r = 0.80$, $p < 0.0001$ and Doppler: $r = 0.85$, $p < 0.0001$). The authors concluded that tissue MR imaging is a feasible method to assess Ea and that combining E and Ea allowed similar estimation of filling pressure by MR and Doppler, in good agreement with invasive measurement.

Malm et al. (2005)
The authors aimed to evaluate whether the use of apical long-axis (APLAX) rather than two-chamber (2CH) view, in combination with four-chamber (4CH) view, improved accuracy of biplane echocardiographic measurements of left ventricular (LV) ejection fraction (EF), using magnetic resonance imaging (MRI) as a reference standard. One hundred consecutive cardiac patients underwent cardiac MRI and 2D-echocardiography. Standard apical LV views were digitally acquired with baseline tissue harmonic imaging and low-power contrast echocardiography. Echocardiographic and MRI LV volumes were calculated by manual tracing and disc summation methods. Feasibility for biplane volume measurements increased with the use of APLAX. Precontrast limits of agreement (LOA) for EF compared to MRI were -19.1 to 9.0 % (EF units) using 2CH, narrowing to -14.6 to 6.7% using the APLAX. With contrast, corresponding LOAs narrowed from -10.5 to 6.1%, to -7.3 to 3.8%, respectively. The improved accuracy with APLAX was evident regardless of image quality, previous MI and regional LV dyssynergy. Both intra- and interobserver variability improved by substituting 2CH with APLAX view. Using APLAX rather than 2CH in combination with 4CH view improved feasibility, accuracy and reproducibility of biplane echocardiographic EF measurements in cardiac patients, even with optimization of endocardial borders by contrast, all using CMRI as a reference standard.

Lim et al. (2005)
This study aimed to evaluate the accuracy of low-power contrast echocardiography (CE) to assess LV remodeling after AMI compared with unenhanced harmonic echocardiography (HE). A total of 36 consecutive patients underwent HE, CE (SonoVue), and cardiovascular magnetic resonance (CMR) imaging 7 to 10 days after AMI. Left ventricular ejection fraction (LVEF), endsystolic volume (LVESV), and end-diastolic volume (LVEDV) were assessed. Absolute differences for LVESV and LVEDV between CMR and CE were significantly smaller than those between CMR and HE. CE estimate of LVEF more accurately classified patients into LVEF < 35%, 35% to 45%, and > 45% (agreement, 83%; kappa = 0.66 with CMR) compared with HE (agreement, 69%; kappa = 0.33 with CMR). The authors concluded that low-power CE is more accurate than HE for estimating LV remodeling after AMI, using CMR as a reference standard.

Westenberg et al. (2005)
In this study, authors sought to quantify the exact flow through the mitral valve with a 3-directional velocity-encoded MRI approach. Ten patients with severe mitral valve regurgitation (class 3-4+ with echocardiography) resulting from systolic restrictive motion of both leaflets (Carpentier IIIb) which were selected for valve repair and 10 healthy volunteers without cardiac valvular disease confirmed with echocardiography were included in this study. The intra-ventricular flow was sampled with a radial stack of six acquisition planes parallel to the long-axis of the left ventricle. Three-directional velocity-encoded MRI was performed resulting in the intra-ventricular flow velocity vector field for 30 phases during the cardiac cycle. The position of the mitral valvular plane in this vector field was indicated manually for each phase. Velocity values perpendicular to this plane determined the flow through the mitral valve. Both the 3-directional encoded mitral valve flow and the 1-directional encoded mitral valve flow were compared with the flow determined with MRI at the ascending aorta. One-directional velocity-encoded MRI showed a mean overestimation ($P < 0.01$) of 25 ml/cycle compared to the aortic flow. Correlation was very poor ($r(P) = 0.15$, $P = 0.68$). The 3-directional velocity-encoded MRI on the other hand, showed no over/underestimation and a good correlation ($r(P) = 0.91$, $P < 0.01$ for volunteers, $r(P) = 0.90$, $P < 0.01$ for patients). The regurgitant flow fractions were between 3 and 30%. The authors concluded that with 3-directional velocity-encoded MRI, measurement of the flow through the mitral valve is accurate and reproducible.

Grothues et al. (2004)
The authors sought to determine the interstudy reproducibility of measurements of right ventricular (RV) volumes, function, and mass with CMRI and compare it with correspondent LV values. Sixty subjects (47 men; 20 healthy volunteers, 20 patients with heart failure, 20 patients with ventricular hypertrophy) underwent 2 CMRI studies for assessment of RV measurements with a minimum time interval between each study. The overall interstudy reproducibility (range between groups) for the RV was 6.2% (4.2%-7.8%) for end-diastolic volume, 14.1% (8.1%-18.1%) for end-systolic volume, 8.3% (4.3%-10.4%) for ejection fraction (EF), and 8.7% (7.8%-9.4%) for RV mass. RV reproducibility was not as good as for the LV for all measures in all 3 groups, but this was only statistically significant for EF ($P < .01$).

The authors concluded that CMRI showed good interstudy reproducibility for RV function parameters in healthy subjects, patients with heart failure, and patients with hypertrophy, which suggests that CMRI is reliable for serial RV assessment.

Lin et al. (2004)
The purpose of this study was to evaluate the reliability of the pressure half-time (PHT) method for estimating mitral valve areas (MVAs) by velocity-encoded cardiovascular magnetic resonance (VE-CMR) and to compare the method with paired Doppler ultrasound. Seventeen patients with mitral stenosis underwent echocardiography and CMR. Using VE-CMR, MVA was estimated by PHT method. Additionally, peak E and peak A velocities were defined. Interobserver repeatability of VE-CMR was evaluated. By Doppler, MVAs ranged from 0.87 to 4.49 cm^2; by CMR, 0.91 to 2.70 cm^2 correlating well between modalities ($r = 0.86$). The correlation coefficient for peak E and peak A between modalities was 0.81 and 0.89, respectively. Velocity-encoded CMR data analysis provided robust, repeatable estimates of peak E, peak A, and MVA ($r = 0.99$, 0.99, and 0.96, respectively). The authors concluded that velocity-encoded cardiovascular magnetic resonance can be used routinely as a robust tool to quantify MVA via mitral flow velocity analysis with PHT method.

Li et al. (2003)
The purpose of this study was to compare the noninvasive assessment of severity of pulmonary regurgitation with Doppler echocardiography versus cardiovascular magnetic resonance imaging (CMR) in adult patients with repaired tetralogy of Fallot (rTOF). The authors studied 52 (22 females) consecutive patients (aged 32 ± 2 years, 23 ± 5 years after rTOF) using Doppler echocardiography and compared these findings with CMR. From the continuous-wave Doppler trace, the duration of pulmonary regurgitation and of total diastole was measured and the ratio between the 2 was defined as pulmonary regurgitation index (PRi). Pulmonary regurgitant fraction (PRF) was assessed with flow phase velocity mapping with CMR.

Patients were divided into 2 groups according to the median value (24.5%) of PRF measured by CMR: Group I (26 patients) with PRF ± 24.5% and Group II with PRF > 24.5%. There was no difference between patients' age, sex, or age at repair between the 2 groups. More patients from Group II had a right ventricular outflow or transannular patch repair compared to Group I (12/26 [46%] versus 6/26 [23%], P < .01). Mean pulmonary regurgitation time was shorter (340 ± 60 versus 440 ± 135 ms, P = .001) and PRi was lower (0.61 ± 0.11versus0.91 ± 0.11, P < .001) in Group II compared to Group I. Color Doppler regurgitant jet was also broader in Group II (1.4 ± 0.4 versus 0.7 ± 0.5 cm, P < .001), signifying more severe pulmonary regurgitation. Doppler-measured PRi correlated closely with CMR regurgitant fraction (r = -0.82, P < .001) and with color Doppler pulmonary regurgitant jet width (r = -0.66, P < .001); the latter correlated with PRF assessed with CMR (r = 0.72, P < .001). A PRi < 0.77 had 100% sensitivity and 84.6% specificity for identifying patients with pulmonary regurgitant fraction > 24.5%, with a predictive accuracy of 95%. Furthermore, echocardiographically-assessed right ventricular end-diastolic dimensions correlated with CMR end-diastolic volume index (r = 0.49, P < .001). The authors concluded that the severity of pulmonary regurgitation and its effects on right ventricular dimensions in these patients can be assessed noninvasively by Doppler echocardiography and CMR, with reasonable agreement between the 2 techniques.

Powell et al. (2003)

The aim of this study was to prospectively evaluate the accuracy, reproducibility, and interobserver variability of phase-velocity cine magnetic resonance imaging (PVC MRI) measurements of Qp/Qs in subjects with a known shunt. Oximetry at catheterization was selected for comparison because, according to the authors, this remains the most widely accepted clinical standard [as of the date of the study]. From June 1999 to March 2002, 20 subjects were prospectively enrolled in the study (12 female and 8 male subjects, mean age 27± 13 years [range 9 to 52]). No subject had significant cardiac disease other than a secundum atrial septal defect or patent foramen ovale. All subjects completed the MRI protocol without complications and underwent cardiac catheterization within a median of 2 days (range 0 to 32). The authors concluded that this study prospectively demonstrated close agreement between PVC MRI and invasive oximetry measurements of Qp/Qs in 20 patients with interatrial communications.

Caruthers et al. (2003)

The purposes of this study were to define the reliability of velocity-encoded CMR as a routine method for quantifying stenotic aortic valve area, to compare this method with the accepted standard, and to evaluate its reproducibility. Patients (n = 24) with aortic stenosis (ranging from 0.5 to 1.8 cm2) were imaged with CMR and echocardiography. Velocity-encoded CMR was used to obtain velocity information in the aorta and left ventricular outflow tract. From this flow data, pressure gradients were estimated by means of the modified Bernoulli equation, and VTIs were calculated to estimate aortic valve orifice dimensions by means of the continuity equation. The correlation coefficients between modalities for pressure gradients were r = 0.83 for peak and r = 0.87 for mean. The measurements of VTI correlated well, leading to an overall strong correlation between echocardiography and MRI modalities for the estimation of valve dimension (r = 0.83). For 5 subjects, the CMR examination was repeated using the best approach. The repeat calculations of valve size correlated well (r = 0.94). The authors concluded that velocity-encoded CMR can be used as a reliable, user-friendly tool to evaluate stenotic aortic valves. The measurements of pressure gradients, VTIs, and the valve dimension correlate well with the accepted standard of Doppler ultrasound.

Nanda et al. (2003)

This study was conducted to assess the ability of a new echocardiographic contrast agent, Imagent (perflexane lipid microspheres; to improve endocardial border delineation (EBD) and assessment of segmental wall motion (SWM). This was achieved by analysis of inter-reader agreement by echocardiography and comparison with an independent imaging technique, magnetic resonance imaging (MRI). Two separate, independent, prospective, randomized, controlled, multicenter trials were conducted at 26 centers and included a total of 409 efficacy-evaluable patients. In Study A 206 patients were randomized to receive either Imagent or saline and in Study B, 203 patients received Imagent with a subset of 26 of 203 patients imaged by both echocardiography and MRI. Patients were referred for echocardiograms for a range of indications including the assessment of regional and global LV function. All patients were required to have suboptimal baseline images using fundamental imaging. Imagent, a suspension of perfluorohexane-filled spheres with flexible lipid shells, was administered as an IV bolus at 0.125 mg/kg body weight. Gated MRI studies were performed within 48 hours of dosing in the subset of 26 subjects. For comparison to MRI, the results from echo readers 4, 5, and 6 were each compared with a single independent MRI reader. Blinded review of the noncontrast echo examinations resulted in agreement with MRI derived SWM scores in 15% of the segments. The administration of Imagent improved this agreement to 47%, of the segments ($P \leq 0.0005$ for each blinded reader). Use of Imagent during echocardiographic imaging improves EBD, providing a significant improvement in inter-reader agreement in SWM evaluation with echo and greater than a threefold improvement in SWM scoring accuracy with MRI. This study (B) has severe design drawbacks and is not really an RCT. No separate information for the 26 patients selected for MRI re: demographics, method of selection, etc, was given. The authors also state that MRI has become an alternative method for the assessment of wall motion, proving particularly beneficial in patients where suboptimal image quality is obtained during echocardiographic assessment.

Grothues et al. (2002)
The authors aimed to make a direct comparison of the interstudy reproducibility of both CMRI and echocardiography methods in the same subjects. A total of 60 subjects (normal volunteers [n = 0], or patients with heart failure [n = 20] or LV hypertrophy [n = 20]) underwent 2 CMRs and 2 echocardiographic studies for assessment of LV volumes, function, and mass. The interstudy reproducibility coefficient of variability was superior for CMR in all groups for all parameters. The authors concluded that statistical significance was reached for end-systolic volume (4.4% to 9.2% versus 13.7% to 20.3%, $p < 0.001$), ejection fraction.

Aaberg (2001)
One hundred patients with refractory angina were randomized 1:1 to TMR (CO2 laser) and medical treatment, or medical treatment alone. Technetium 99m (99mTc)-tetrofosmin myocardial perfusion tomography (SPECT), quantitative myocardial perfusion gated SPECT (QGSPECT), technetium 99m (99mTc) multiple gated acquisition radionuclide ventriculography (MUGA) and cine-magnetic resonance imaging (cine-MRI) were performed at baseline and after 3 and 12 months. Following TMR, a slight reduction in left ventricular ejection fraction (LVEF) ($p < 0.05$) was observed (MUGA and QGSPECT) compared to baseline. Inclusion of incomplete studies (QGSPECT) revealed a significant reduction in LVEF and increase in left ventricular end-diastolic volume (LVEDV) ($p < 0.05$) compared to a control group. Otherwise, no between-group comparisons showed statistically significant differences. The authors concluded that TMR did not improve myocardial perfusion, but led to a reduction in LVEF and increase in LVEDV, however not significantly different from the control group.

Arheden et al. (1999)

The authors aimed at investigating the agreement between two noninvasive methods, magnetic resonance (MR) velocity mapping and first-pass radionuclide angiography, to quantify the pulmonary-to-systemic blood flow ratio (QP/QS) in adults, adolescents, and children with left-to-right cardiac shunts. The accuracy and precision of MR velocity mapping were studied in 12 control subjects (six men, six women) and in a phantom. MR velocity mapping and radionuclide angiography were performed on the same day in 24 patients (16 adults, two adolescents, six children; five male patients, 19 female patients). The mean error in QP/QS at MR velocity mapping in phantom experiments was -1% ± 1 (mean ± SD). In control subjects, QP/QS at MR velocity mapping was 1.03 ± 0.03, and the cardiac index was 3.1 L/min/m^2 ± 0.2 and 3.2 L/min/m^2 ± 0.3 for women and men, respectively. In patients, QP/QS at radionuclide angiography was 14% ± 13, higher than at MR velocity mapping. Interobserver variability was four times higher for radionuclide angiography compared with MR velocity mapping, 0% + 16 versus 0% ± 4 (n = 12). The difference between repeated MR flow measurements in the same vessel was -1% ± 5 (n = 36). The authors concluded that the data suggested that MR velocity mapping is accurate and precise for measurements of shunt size over the whole range of possible QP/QS values.

Berg (1998)

To compare the effects of stented and stentless prostheses on early hemodynamic function and late left ventricular mass regression, a prospective randomized clinical trial was conducted. Following valve sizing, 20 patients were randomized to receive a Carpentier-Edwards SAV stented bioprosthesis (mean annular size-25.3 mm, mean valve size-23 mm) of which eight also had bypass grafts. Twenty patients were randomized to receive a Toronto Stentless Porcine Valve (SPV), mean annular size-25.5 mm, mean valve size-26 mm, of which nine had bypass grafts. The stentless valve group had a longer ischemic time (77.9 ± 20.9 min versus 60.9 ± 21.9 min) and bypass time (101.7 ± 27.1 min versus 82.9 ± 20.2 min). Using continuous cardiac output monitoring, no statistically significant differences were found in early hemodynamic indices although the stentless group required less inotropes and had a shorter ventilation time (16.1 ± 4.2 hrs versus 55.2 ± 104.9 hrs) and intensive care stay (1.1 ± 0.2 days versus 4.6 ± 8.3 days). Mean and peak aortic gradients one week postoperatively were lower in the stentless group (5.6 ± 3 mmHg versus 8.9 ± 2.3 mmHg and 12.5 ± 7.8 mmHg versus 24.4 ± 8.8 mmHg respectively). CMRI at one week and six months was used to measure stroke volumes, ejection fractions, end diastolic muscle mass and end systolic muscle mass indices. CMRI showed a 15% reduction in the end systolic muscle mass index in the stented group but a greater reduction of 29% in the stentless group. The authors concluded that this study showed that despite requiring a more demanding technique of insertion, aortic valve replacement with the Toronto stentless porcine valve can produce satisfactory early clinical results. In this study CMRI was the standard for measurement of stroke volumes, ejection fractions, end diastolic muscle mass and end systolic muscle mass indices and was not compared to any other modality

Hundley et al. (1995b)

Velocity-encoded, phase-difference magnetic resonance imaging (MRI) has been used to measure flow in the aorta, as well as in the pulmonary, carotid, and renal arteries, and the authors noted that these measurements have not [to present] been validated against currently accepted invasive techniques. To determine the accuracy of velocity-encoded, phase-difference MRI measurements of cardiac output, 23 subjects (11 men and 12 women, aged 15 to 72 years) underwent velocity-encoded, phase-difference MRI measurements of cardiac output in the proximal aorta, followed immediately by cardiac catheterization, with measurement of cardiac output by the Fick principle and by thermodilution. For MRI, Fick, and thermodilution measurements, stroke volume was calculated by dividing cardiac output by heart rate. The magnetic resonance images were acquired in 1 to 3 minutes. For all patients, the agreement between measurements of stroke volume was 3 ± 9 ml for MRI and Fick, -3 ± 11 ml for MRI and thermodilution, and 0 ± 8 ml for MRI and the average of Fick and thermodilution. The authors concluded that compared with standard invasive measurements, velocity-encoded, phase-difference MRI can accurately and rapidly determine cardiac output.

Hundley et al. (1995a)
This study was done to determine whether MRI can reliably measure the magnitude of mitral regurgitation and evaluate the effect of regurgitation on left ventricular volumes and systolic function. The authors noted that, in the patient with mitral regurgitation who is being considered for valvular surgery, cardiac catheterization is usually performed to quantify the severity of regurgitation and to determine its influence on left ventricular volumes and systolic function. They also noted that magnetic resonance imaging (MRI) potentially provides a rapid, noninvasive method of acquiring these data.

Twenty-three subjects (14 women and 9 men 15 to 72 years of age) with (n = 17) or without (n = 6) mitral regurgitation underwent MRI scanning followed immediately by cardiac catheterization. The presence (or absence) of valvular regurgitation was determined, and left ventricular volumes and regurgitant fraction were quantified during each procedure. There was excellent correlation between invasive and MRI assessments of left ventricular end-diastolic (r = .95) and end-systolic (r = .95) volumes and regurgitant fraction (r = .96). All MRI examinations were completed in < 28 minutes. The authors concluded that, in the patient with mitral regurgitation, MRI compares favorably with cardiac catheterization for assessment of the magnitude of regurgitation and its influence on left ventricular volumes and systolic function.

Heidenreich et al. (1995)
The authors wrote that velocity-encoded cine-magnetic resonance imaging (VEC-MRI) was a new method for quantitation of blood flow with the potential to measure high-velocity jets across stenotic valves. The objective of their study was to evaluate the ability of VEC-MRI to measure transmitral velocity in patients with mitral stenosis. Sixteen patients with known mitral stenosis were studied. A 1.5 Tesla superconducting magnet was used to obtain velocity-encoded images in the left ventricular short-axis plane. Images were obtained throughout the cardiac cycle at 3 consecutive slices beginning proximal to the mitral coaptation point. To determine the optimal slice thickness for MRI imaging, both 10 mm and 5 mm thicknesses were used. Echocardiography including continuous-wave Doppler was performed on every patient within 2 hours of MRI imaging. Peak velocity was determined for both VEC-MRI and Doppler-echo images. Two observers independently measured the VEC-MRI mitral inflow velocities. Of the 16 patients, imaged data were incomplete in only 1 study, and all images were adequate for analysis. Strong correlations were found for measurements of mitral valve gradient for both 10 mm (peak r = 0.89, mean r = 0.84) and 5 mm (peak r = 0.82, mean r = 0.95) slice thicknesses. Measurements of peak velocity with VEC-MRI (10 mm) agreed well with Doppler: mean 1.46 m/s, mean of differences (Doppler MRI) 0.38 m/s, standard deviation of differences 0.2 m/s. The authors concluded that their findings suggested that VEC-MRI can noninvasively determine the severity of mitral stenosis.

Fujita et al. (1994)

The authors evaluated the feasibility of velocity-encoded cine nuclear magnetic resonance (NMR) imaging to measure regurgitant volume and regurgitant fraction in patients with mitral regurgitation. They hypothesized that the difference between mitral inflow and aortic systolic flow provides the regurgitant volume in the setting of mitral regurgitation. Using velocity-encoded cine NMR imaging at a magnet field strength of 1.5 T and color Doppler echocardiography, 19 patients with isolated mitral regurgitation and 10 normal subjects were studied. Velocity-encoded cine NMR images were acquired in the short-axis plane of the ascending aorta and from the short-axis plane of the left ventricle at the level of the mitral annulus. Two independent observers measured the ascending aortic flow volume and left ventricular inflow volume to calculate the regurgitant volume as the difference between left ventricular inflow volume and aortic flow volume, and the regurgitant fraction was calculated. Using accepted criteria of color flow Doppler imaging and spectral analysis, the severity of mitral regurgitation was qualitatively graded as mild, moderate or severe and compared with regurgitant volume and regurgitant fraction, as determined by velocity-encoded cine NMR imaging. In normal subjects the regurgitant volume was -6 ± 345 ml/min (mean ± SD). In patients with mild, moderate and severe mitral regurgitation, the regurgitant volume was 156 ± 203, 1,384 ± 437 and 4,763 ± 2,449 ml/min, respectively. In normal subjects the regurgitant fraction was 0.7 ± 6.1%. In patients with mild, moderate and severe mitral regurgitation, the regurgitant fraction was 3.1 ± 3.4%, 24.5 ± 8.9% and 48.6 ± 7.6%, respectively.

The regurgitant fraction correlated well with the echocardiographic severity of mitral regurgitation (r = 0.87). Interobserver reproducibility for regurgitant volume and regurgitant fraction were excellent (r = 0.99, SEE = 238 ml; r = 0.98, SEE = 4.1%, respectively.) The authors concluded that these findings suggest that velocity-encoded NMR imaging can be used to estimate regurgitant volume and regurgitant fraction in patients with mitral regurgitation and can discriminate patients with moderate or severe mitral regurgitation from normal subjects and patients with mild regurgitation. Thus they believe it may be useful for monitoring the effect of therapy intended to reduce the severity of mitral regurgitation.

Eichenberger et al. (1993)

The purpose of this study was to determine the feasibility and accuracy of velocity-encoded cine MR for estimating pressure gradients across the aortic valve in patients with aortic stenosis. Pressure gradients across the aortic valve (AV) due to stenosis of the valve must be measured accurately to evaluate the functional severity of the stenosis. Velocity-encoded cine MR has been used to quantify blood flow and flow direction and, more recently, the regurgitant fraction in aortic regurgitation. The authors employed velocity-encoded cine MR to measure flow velocity and determine pressure gradients across the aortic valve in 19 subjects. The pressure gradient (delta P) was estimated from the simplified Bernoulli equation by using the maximum instantaneous aortic jet velocity (V_{max}: ΔP (mm Hg) = $4V^2_{max}$ (m/sec). Maximum and mean systolic pressure gradients determined by using velocity-encoded cine MR were 3-148 mm Hg and 2-87 mm Hg, respectively, for all subjects. The pressure gradients correlated closely with gradients determined by using established methods: Doppler echocardiography and cardiac catheterization. Correlation coefficients (r) were .96 (y = 0.94x - 1.9) and .97 (y = 0.97x + 0.5), respectively. The authors concluded that velocity-encoded cine MR imaging provides a noninvasive and accurate means for quantifying the severity of valvular aortic stenosis.

Honda (1993)

Aortic regurgitation (AR) in five healthy volunteers and 26 patients (mean age, 60.3 years; range, 25-83 years) was quantitatively measured with magnetic resonance (MR) imaging velocity mapping. Cine transverse images of the ascending aorta (32 phases per cardiac cycle) were acquired by using a gradient-echo sequence with a velocity-encoding bipolar pulse applied in the section-selection direction with a 1.5-T MR imaging unit. Aortic flow was calculated by integrating the product of area and mean velocity of the ascending aorta at each phase over a cardiac cycle. The negative and positive velocity values indicated antegrade and regurgitant flow, respectively, which allowed calculation of forward and regurgitant flow. Inter- and intraobserver variation of regurgitant fraction (RF) measurement was small (r = .956, standard error of the estimate [SEE] = 1.2%, n = 31; and r = .998, SEE = 0.35%, n = 10, respectively). RF determined with MR imaging agreed well with Doppler echocardiographic (n = 26) and aortographic (n = 9) grading of AR. The authors conclude that reproducible, quantitative, and noninvasive measurement of AR is possible with MR velocity mapping.

Kilner et al. (1993)
The objective of this study was validation of MR jet velocity mapping in patients with cardiac valve stenosis. The authors used a 0.5-T Picker MR machine to measure peak poststenotic jet velocity in 15 consecutive patients recruited with known valve disease (six mitral stenosis, three of these restudied after valvuloplasty, and 11 aortic stenosis). On the same day as the MR study, these patients underwent independent Doppler echocardiographic measurement of peak jet velocity. The results of 10 further MR investigations of aortic stenosis are also reported and compared with Doppler studies performed within 6 months. To reiterate, of 26 patients 14-79 years old (mean age, 53 years), 15 were recruited prospectively for the study, being known to have mitral and/or aortic stenosis. Of these, five had mitral stenosis. A total of 29 MRI studies were performed, 28 (97%) produced interpretable velocity maps, the one failure being attributed to misplacement of the imaging slice in a case of severe aortic stenosis.

Agreement between MR and Doppler measurements of peak jet velocity in the recruited group was as follows: n = 18; range, 1.4-6.1 m/sec; mean, 3 m/sec; mean of differences (MR-Doppler), 0.23 m/sec; standard deviation of differences, 0.49 m/sec. The authors concluded that *in vivo* MR peak jet velocity measurements agree well with those made by Doppler ultrasound. They also surmised that the technique, which is not subject to restricted windows of access and has potential for further refinements, could contribute to improved evaluation of stenoses, especially at locations where ultrasonic access is limited.

Kizilbash et al. (1993)
The authors compared quantitative Doppler echocardiography and cine magnetic resonance imaging for calculation of regurgitant volume and regurgitant fraction in mitral regurgitation. The study population consisted of 22 subjects (14 men and 8 women, 24 to 68 years of age) referred for echocardiography for evaluation of MR. In these patients, MR was associated with mitral valve prolapse (n = 9), dilated cardiomyopathy (n = 5), and ischemic heart disease (n 5 4). Forward stroke volume was measured by velocity encoded phase difference sequences positioned perpendicular to the ascending aorta, well above the aortic valve and coronary ostia. For flow sequences, slices of 10 mm thickness were obtained with a 256 3 192 matrix, 35-cm field-of-view, 60° flip angle, 460 to 500 ms repetition time, and 5 ms echo time. After first-order Fourier transformation, motion-compensated reference scan and the velocity sensitized scan were generated.

From the 2 sets of images (magnitude and corresponding phase image), velocity maps were obtained by a pixel-to-pixel subtraction method. Regurgitant volume was calculated as the difference between the total left ventricular stroke and the forward stroke volume. Regurgitant fraction was calculated as regurgitant volume divided by total stroke volume. MRI and quantitative Doppler studies were completed in all subjects. Overall, regurgitant volume by quantitative Doppler correlated well with MRI ($r = 0.92$) with a mean difference of -3± 13 ml. Regurgitant fraction by quantitative Doppler also correlated with MRI ($r = 0.82$) with a mean difference of -7± 11%. Quantitative Doppler correctly distinguished all patients with severe MR (regurgitant volume ~50 ml) from those with mild to moderate MR. A good correlation was present between the 2 methods with some scatter in patients with severe mitral regurgitation and high regurgitant volumes. The authors concluded that quantitative Doppler is a reliable method of quantifying MR and that it correctly identifies patients with severe MR who may require surgical intervention.

White (1988)

To assess relative capabilities of magnetic resonance (MR) imaging and two-dimensional echocardiography (2DE) for evaluating regional contractile dysfunction in the left ventricle after a myocardial infarction, results from 22 concurrent MR (orthogonal-transaxial, ECG-gated, multiphasic, single-spin echo) and 2DE examinations were compared. By means of the same 11-segment LV description, MR and 2DE examinations were independently scored segment by segment for residual wall motion (point scores: 2 = normal, 1 = hypokinesia, 0 = akinesia, and -1 = dyskinesia). Significant correlation between MR and 2DE scoring was found throughout most of the left anterior descending (LAD) distribution, but right coronary artery (RCA) distribution (i.e., middle-posterior segment not well seen) could not be fully evaluated by MR imaging. When cumulative scores for the 10 segments mutually evaluated were used to derive measures of global residual LV function (i.e., score quotient [SQ] = accumulated points divided by 20 total possible points), MR SQ correlated well overall with both 2DE SQ ($r = 0.82$; $p < 0.05$) and ejection fraction (EF) from ventriculography ($r = 0.86$, $p < 0.05$versusr = 0.88, $p < 0.05$ for 2DE SQ compared with EF). MR evaluation of segmental wall motion was relatively stronger in the LAD distribution (MR SQ compared with 2DE SQ: $r = 0.86$, $p < 0.05$; MR SQ compared with EF: $r = 0.96$, $p < 0.05$) than in the RCA distribution ($r = 0.06$, $p \geq 0.05$ and $r = 0.62$, $p \geq 0.05$, respectively). For 2DE, regional variations were not as evident (2DE SQ compared with EF: $r = 0.90$, $p < 0.05$ for LAD and $r = 0.81$, $p < 0.05$ for RCA). The authors conclude that, for segmental evaluation of wall motion after myocardial infarction, MR imaging (transaxial, multiphasic) appears to be comparable to 2DE overall but superior in LAD distribution and inferior in RCA distribution.

The secondary request

CMS performed a literature search on 5/18/2009 utilizing PubMed for search terms involving MRI and pacemakers. We also looked to see if there are any pacemakers or cardioverter-defibrillators approved by FDA as safe for use in an MRI environment. Our search failed to produce any evidence that any such devices exist at this time.

Not surprisingly, we found no evidence that would support the effect of a nonexistent device on health outcomes in Medicare beneficiaries.

4. MEDCAC

A Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) meeting was not convened on either issue.

5. Evidence-based guidelines

ACR Appropriateness Criteria® suspected congenital heart disease in the adult.

Magnetic Resonance Imaging

MRI is useful for evaluating CHD. Without the concerns related to exposure to ionizing radiation or the use of nephrotoxic iodinated contrast agents, it can provide morphologic and functional information essential for detecting and managing CHD. Traditional "black-blood" techniques (e.g., spin-echo MRI and double inversion recovery fast spin echo) are useful for delineating cardiac and pericardiac anatomy. "Bright-blood" techniques, notably using newer cine steady-state free-precession pulse sequences, can demonstrate flow abnormalities (e.g., a flow jet) related to lesions such as an interventricular or interatrial septal defect, valvular insufficiency, valvular stenosis, or coarctation. Defining the plane in which the jet velocity is maximal can be difficult with MRI. However, with improvements in software and real-time localization algorithms, this is becoming easier. Parallel imaging and newer k-space schemes can shorten the acquisition times in most instances such that cine bright-blood imaging can be performed during a short breath hold. Bright-blood techniques also enable volumetric coverage of cardiac chambers for determining cardiac metrics such as ventricular volumes, ejection fractions, and myocardial mass. Longer acquisitions as may be required for coronary magnetic resonance angiography (MRA) are typically performed using navigator respiratory gating methods.

Phase contrast techniques demonstrate directional blood flow information for improved identification of subtle intra- or extracardiac shunt lesions. Phase contrast also allows quantification of blood flow (e.g., estimation of the ratio of pulmonary to systemic blood flow [Qp/Qs]), regurgitant fractions, and pressure gradients across valves.

MRI has been used for diagnosing essentially all congenital heart and great-vessel abnormalities. Conventional spin-echo MRI has been shown to have very high sensitivity and specificity for diagnosing common CHD. At a specificity of 90%, spin echo was found to have high sensitivity in diagnosing great-vessel relationships (100%), thoracic aortic abnormalities (94%), ASDs (91%), VSDs (100%), visceroatrial situs (100%), and the cardiac loop (100%). Pulmonary and systemic venous anomalies and right ventricular outflow obstructions are also detected with high sensitivity. Vascular rings can also be accurately diagnosed without the need for angiography. MRI can also be performed using 3D techniques for high spatial-resolution Gd-enhanced 3-D MRA, or to provide volumetric coverage of cardiac chambers. Time-resolved MRA was found to provide a very high diagnostic value (92% of diagnostic parameters assessed) that included thoracic vascular anatomy, sequential cardiac anatomy, and shunt detection with high sensitivity (93%-100%) and high specificity (87%-100%).

Gradient-echo imaging acquisition viewed in a cine format facilitates physiologic measurements, including stroke volume, ejection fraction, and wall motion of both ventricles. Blood flow, valve gradients, shunt flow, regurgitant flow, and pulmonary flow can all be measured using velocity-encoded cine techniques.

MRI seems to be ideally suited for evaluating adults with suspected or known CHD. Although claustrophobia in the gantry may require sedation in a few patients, the study is noninvasive, and image quality is not affected by body habitus. MRI can provide high-spatial-resolution images even in more complex CHD without the limitation of imaging "windows" or plane as experienced during echocardiography. MRI images can be obtained in essentially any plane for improved 3-dimensional presentation of cardiac anatomy. MRI is useful as well in evaluating the postoperative patients with CHD, whether it is a palliative procedure, a surgically created conduit, or reconstructed great vessels.

(Accessed May 27, 2009 at http://www.guidelines.gov/summary/summary.aspx?doc_id=11557&nbr=005988&string=%22Magnetic+resonance%22+AND+%22blood+flow%22)

6. Professional Society Position Statements

Various professional societies expressed positions via the request or public comment.

As noted in the request, the American College of Radiology (ACR), the American College of Cardiology (ACC), North American Society for Cardiovascular Imaging (NASCI), and the Society for Cardiovascular Magnetic Resonance (SCMR) strongly believe that MRI flow quantification is more reliable and reproducible and leads to better treatment decisions than alternative diagnostic techniques and therefore request that the blood flow measurement be removed from the list of non-covered indications.

The American Heart Association (AHA) believes that blood flow quantification is a valuable diagnostic tool when utilized as a component of a broader cardiac MRI examination and it is an accepted and necessary part of clinical practice when evaluating patients for a known or suspected congenital or valvular heart disease.

7. Expert Opinion

We did not solicit any expert opinions on the use of Cardiac MRI and blood flow measures.

8. Public Comments

Initial Comment Periods:
January 20, 2009 through February 19, 2009
CMS received 86 public comments during the first public comment period. All of the comments supported removing the reference to blood flow measurement from the nationally non-covered indications and including it in the covered indications. Comments were received from cardiologists, radiologists, electrophysiologists, academicians, researchers, and providers, in addition to a comment from the requestor, American Health Insurance Plans (AHIP), and the Cardiology Advocacy Alliance (CAA). Any articles submitted with these public comments were not unique to those submitted by the requestor of identified by CMS during its literature review.

In addition, CMS received a request from Medtronic, Inc. in which it recommended modifying the Contraindications section to permit coverage of MRI when devices such as cardiac pacemakers have been designed, tested and FDA labeled for use in the MRI environment. CMS broadened the scope of this review and solicited for comments for an additional thirty days on this aspect of the request.

March 16, 2009 through April 15, 2009
CMS received 6 additional public comments during this public comment period, including comments from the American Heart Association (AHA), a private insurer, AHIP, academicians, and industry, in addition to a comment from the requestor Medtronic. Most comments that addressed Medtronic's request were opposed to modification of the contraindication section.

Proposed Decision Comment Period: June 30, 2009 through July 30, 2009

CMS received eight timely public comments on the proposed decision. Of the comments, two were from physicians, two were from cardiac device manufacturers, one was from a national association of health insurers, one was from a manufacturers association, one was from the physician specialty societies comprising the original requestor, and one was from a national radiology clinic. Any additional evidence submitted with public comments is addressed below.

As this NCA is considering two distinct requests we will discuss them separately here.

Comments
All comments on the primary request, i.e. coverage of MRI for the assessment of blood flow, supported this aspect of the proposed decision.

Response
We appreciate their support.

Comments were split on the secondary request, i.e. removal of the noncoverage of MRI for beneficiaries who have implanted devices such as pacemakers or implantable cardioverter-defibrillators that have been approved by FDA as safe for use in an MRI environment. Four comments, including the secondary requestor (Medtronic) favored removal of noncoverage while two favored continuing noncoverage.

Comments

The comments favoring removal the contraindication suggested coverage in circumstances when they believe that the potential benefit outweighs the potential harm and other imaging is not suitable. One commenter suggests that keeping a registry open to add any untoward events may be a better strategy. The commenters cite personal experiences to illustrate the use of MRI for this patient population. Commenters (including one device manufacturer) who favored continuing noncoverage cited the lack of FDA approval of claims of safety of these devices in the MRI environment and the need for rigorous clinical study of this potential use. One commenter believes the risks associated with the use of MRI in this patient population have not been completely characterized or mitigated to justify routine use. They would support reconsideration of this request at a later date if new standards were developed by the ISO/IEC Joint Working Group and AHA's guidelines were changed to support the safe use of MRI in these patient populations. Two commenters ask that we promptly reconsider this NCD if FDA approves such devices.

Response

It is apparent that even the manufacturers of implantable cardiac devices disagree on whether or not the current noncoverage should be removed. While CMS appreciates the commenters' reports of personal experiences, we must accord it less evidentiary weight than evidence from more methodologically rigorous clinical trials. As we noted in the proposed decision, we would expect to receive and review evidence toward a reconsideration request if FDA approves such devices.

One commenter sent in four references, one of which (Kanal et al., 2007) was already discussed in the proposed decision. The remaining three are discussed below. Another commenter submitted two references on computed tomography. We did not review these further as they do not bear on the evidentiary questions posed in this decision.

Levine GN, Gomes AS, Arai AE, Bluemke DA et al. Safety of magnetic resonance imaging in patients with cardiovascular devices: an American Heart Association scientific statement from the Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology, and the Council on Cardiovascular Radiology and Intervention: endorsed by the American College of Cardiology Foundation, the North American Society for Cardiac Imaging, and the Society for Cardiovascular Magnetic Resonance. Circulation. 2007 Dec 11;116(24):2878-91. Epub 2007 Nov 19.

The goal of this article was to state safety recommendations for use of MRI in patients with cardiovascular devices such as pacemakers. The authors state that extensive, although not complete, ex vivo, animal, and clinical data are available from which to generate recommendations regarding the safe performance of MR examination in patients with cardiovascular devices, as well as to ascertain caveats and contraindications regarding MR examination for such patients. This scientific statement is intended to summarize and clarify issues regarding the safety of MR imaging in patients with cardiovascular devices.

The authors and committees recommended

General recommendations:

1) MR examination of non–pacemaker-dependent patients is discouraged and should only be considered in cases in which there is a strong clinical indication and in which the benefits clearly outweigh the risks. MR examination of pacemaker-dependent patients should not be performed unless there are highly compelling circumstances and when the benefits clearly outweigh the risks.

2) MR examination of patients with ICDs should not be performed unless there are highly compelling circumstances and when the benefits clearly outweigh the risks.

3) Scanning should only be performed at extremely experienced centers with expertise in MR imaging and electrophysiology.

4) Establish and document the risk-benefit ratio for the patient.

5) Obtain written and verbal informed consent. Written informed consent should specifically list risks, including (1) pacemaker/ICD dysfunction, (2) pacemaker/ICD damage, (3) arrhythmia, and (4) death.

6) A physician with ACLS and pacemaker/ICD expertise should decide whether it is necessary to reprogram the pacemaker/ICD before the MR examination and should be in attendance for the entire study.

7) A person with expertise in MR physics and safety should be involved with the scan to optimally plan the scan to minimize risk, and consideration should be given to using scanning parameters (e.g., lowest RF power levels, weakest/slowest necessary gradient magnetic fields) that are believed to minimize study risk.

8) Prescanning steps outside the MR environment: For non–pacemaker-dependent patients, pretest pacemaker functions.

9) For pacemaker-dependent patients, pretest pacemaker functions and reprogram to asynchronous mode.

10) For patients with ICDs, pretest ICD functions and disable therapy and detection for tachycardia/bradycardia modes.

11) The patient’s heart rhythm and vital signs should be monitored throughout the MR procedure.

12) Appropriate personnel and a "crash cart," including defibrillator, must be available throughout the procedure to address an adverse event.

13) Maintain visual and voice contact with the patient throughout the procedure.

14) Instruct the patient to alert the MR system operator to any unusual sensations or problems.

After the examination:

1) For non–pacemaker-dependent patients, a physician with electrophysiological expertise should interrogate the pacemaker and reprogram as needed

2) For pacemaker-dependent patients, a physician with electrophysiological expertise should interrogate the pacemaker function and reprogram the pacemaker

3) For patients with ICDs, a physician with electrophysiological expertise should perform postscan device reprogramming and defibrillation threshold testing

The authors concluded with a statement that discussions of device safety are based on research through mid-2006 and are based only on devices that are commercially available as of this writing; recommendations in this statement will not necessarily apply to devices developed in the future. When doubt remains as to the safety of performing an MR examination, the reader is urged to consult a more detailed source of information, such as dedicated Web sites, reference manuals, or, especially, the manufacturer's product information when available. The authors finally stated that because of the increasing use of MR examinations, as well as the increasing number of cardiovascular devices implanted in patients, efforts by industry, working in collaboration with academia, to manufacture devices, including pacemakers and ICDs, that are specifically designed to be safe for MR examination should be continued and intensified.

Sommer T, Naehle, CP, Yang A et al. Strategy for Safe Performance of Extrathoracic Magnetic Resonance Imaging at 1.5 Tesla in the Presence of Cardiac Pacemakers in Non–Pacemaker-Dependent Patients A Prospective Study With 115 Examinations. Circulation. 2006;114: 1285-1292.

The stated purpose of the study was to evaluate a strategy for safe performance of extrathoracic magnetic resonance imaging (MRI) in non-pacemaker-dependent patients with cardiac pacemakers. Inclusion criteria were presence of a cardiac pacemaker and urgent clinical need for an MRI examination. Pacemaker-dependent patients and those requiring examinations of the thoracic region were excluded. The study group consisted of 82 pacemaker patients who underwent a total of 115 MRI examinations at 1.5T. To minimize radiofrequency-related lead heating, the specific absorption rate was limited to 1.5 W/kg. All pacemakers were reprogrammed before MRI: If heart rate was <60 bpm, the asynchronous mode was programmed to avoid magnetic resonance (MR)-induced inhibition; if heart rate was >60 bpm, sense-only mode was used to avoid MR-induced competitive pacing and potential proarrhythmia. Patients were monitored with ECG and pulse oximetry. All pacemakers were interrogated immediately before and after the MRI examination and after 3 months, including measurement of pacing capture threshold (PCT) and serum troponin I levels. All MR examinations were completed safely. Inhibition of pacemaker output or induction of arrhythmias was not observed. PCT increased significantly from pre- to post-MRI (P=0.017). In 2 of 195 leads, an increase in PCT was only detected at follow-up. In 4 of 114 examinations, troponin increased from a normal baseline value to above normal after MRI, and in 1 case (troponin pre-MRI 0.02 ng/mL, post-MRI 0.16 ng/mL), this increase was associated with a significant increase in PCT. The authors concluded that extrathoracic MRI of non-pacemaker-dependent patients can be performed with an acceptable risk-benefit ratio under controlled conditions and by taking both MR- and pacemaker-related precautions.

Gimbel J. Safe, sensible, sagacious: responsible scanning of pacemaker patients. European Heart J. 2005. 26: Online publish-ahead-of-print 9 June 2005

The author, in a letter to the editor, disputes claims made in an editorial of MRI safety in pacemaker patients. The author cites a report that "at least four pacemaker patients have died while undergoing physician supervised MRI" and "in all four cases the patients were not pacemaker dependent."

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally by Medicare (§1869(f)(1)(B) of the Act). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." See §1862(a)(1)(A)of the Act. This section presents the agency’s evaluation of the evidence considered and conclusions reached for the assessment

The Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary’s specific medical problem."

We considered the evidence in the hierarchical framework of Fryback and Thornbury (1991) where Level 2 addresses diagnostic accuracy, sensitivity, and specificity of the test; Level 3 focuses on whether the information produces change in the physician's diagnostic thinking; Level 4 concerns the effect on the patient management plan and Level 5 measures the effect of the diagnostic information on patient outcomes. Most studies have focused on test characteristics and changes in physician diagnostic thinking and have not considered health outcomes, such as mortality or morbidity. We believe that health outcomes are more important than test characteristics.

As a diagnostic test, the MRI scan would not be expected to directly change health outcomes, i.e. there is no evidence that administration of the scan or tracer is therapeutic. Rather, a diagnostic test affects health outcomes through changes in disease management brought about by physician actions taken in response to test results. Such actions may include decisions to treat or withhold treatment, to choose one treatment modality over another, or to choose a different dose or duration of the same treatment. To some extent the usefulness of a test result is constrained by the available management alternatives.

In evaluating diagnostic tests, Mol and colleagues (2003) reported: "Whether or not patients are better off from undergoing a diagnostic test will depend on how test information is used to guide subsequent decisions on starting, stopping or modifying treatment. Consequently, the practical value of a diagnostic test can only be assessed by taking into account subsequent health outcomes." When a proven, well established association or pathway is available, intermediate health outcomes may also be considered. For example, if a particular diagnostic test result can be shown to change patient management and other evidence has demonstrated that those patient management changes improve health outcomes, then those separate sources of evidence may be sufficient to demonstrate positive health outcomes from the diagnostic test.

Questions

The Original Request

Q1. Is the evidence adequate to conclude that MRI assessment of cardiac blood flow informs the diagnosis of cardiac valvular, cardiac shunt, cardiac stroke and ejection volume pathologies, compared to diagnosis of these conditions without MRI assessment of cardiac blood flow?

Q2. Is the evidence adequate to conclude that the MRI assessment of cardiac blood flow improves health outcomes in patients who have valvular pathology, intracardiac shunts, stroke volume abnormalities or reduced ejection fraction?

The Secondary Request

Q3. Is the evidence adequate to conclude that MRI improves health outcomes in Medicare beneficiaries who have implanted devices such as pacemakers or implantable cardioverter-defibrillators that have been approved by FDA as safe for use in an MRI environment?

Summary

The Original Request

As we noted earlier, the original requestors did not ask for national Medicare coverage of MRI for the assessment of blood flow, but specifically requested the removal of the national noncoverage provision so that Medicare contractors could determine coverage for MRI claims without this broad national noncoverage provision. The requestors submitted evidence on MRI assessment of blood flow in the heart because that was the indication that was affected by the change in a code descriptor, as they discussed in their request.

We received electronic copies of journal papers deemed relevant by the requestors. They were published between 1993 and 2007 and represented series of one kind or another (see accompanying table), with no RCTs. Sample sizes were generally in the range of 16-31 with two papers having sample sizes in the 50s and one series having 141 participants. Only one paper (Tanaka 2007) dealt with mostly Medicare age subjects. Eleven of the papers compared CMRI to echocardiography with echocardiography treated as the reference standard in all but one. The other papers involved CMRI alone, or in comparison to cardiac angiography, oximetry, or CT. These papers dealt with a wide range of pathologies relevant to the Medicare aged population 65 years of age or over (AS, MR, MS, cardiac shunts), while some of the submitted references dealt with children and we did not include those for our analysis. Outcome measures ranged over a wide variety of flow volume and velocities regarding the different chambers of the heart and valves. Of note is that all of these papers addressed Q1, the ability of CMRI to influence diagnosis of the varied pathologies mentioned above as compared to other modalities, and that CMRI was considered a viable option for determining cardiac blood flow.

We found additional evidence (Appendix C) dealing with a wide range of pathologies (MI, HF, PAT, dilated cardiomyopathy, cardiac shunts, EBD, hypertension, other). Outcome measures ranged over a wide variety of flow volume and velocities regarding the different chambers of the heart and valves, LV ejection fraction, LV filling pressure, LVESV, LVEDV, LVMI, and EVV, stroke volume and others.

Overall, the body of evidence demonstrates that treating physicians use MRI assessment of cardiac blood flow to manage the care of patients who have one or several cardiovascular diseases. We believe that this management leads to therapeutic interventions, e.g. valve replacement, that improves patient health outcomes. We note the broad support for this use from the public comments and the published guidelines of relevant professional societies.

We believe there is adequate evidence to remove the general noncoverage of blood flow measurement from the NCD. The effect of this change will allow local Medicare contractors to make reasonable and necessary determinations without reliance on this coverage prohibition. As we noted in the Background section, the diagnosis of cardiac valvular disease encompasses the use of a variety of modalities to determine the consequences of many possible causes of dysfunction among four distinct valves. For any individual beneficiary the usefulness of CMRI to guide the treating physician’s management of the beneficiary’s condition may be affected by the beneficiary’s specific medical problem, the availability of results of other diagnostic tests and the expertise of the interpreting physician. We believe in this case that our local administrative contractors, who may more readily obtain this information, can make these determinations within their jurisdictions.

The Secondary Request

The secondary requestor, Medtronic, based its request on the possibility that FDA might in the future approve a pacemaker or implantable cardioverter-defibrillator device as safe for use in an MRI environment. We did not find evidence that MRI improves health outcomes in Medicare beneficiaries who have such implanted devices. This is not surprising, as we are not aware of the existence of any such approved device at this time.

Faris and Shein provided an FDA perspective in a 2006 editorial in Circulation.

In April 2005, the US Food and Drug Administration (FDA) commented on the current research regarding the use of magnetic resonance imaging (MRI) on patients with a pacemaker or implantable Cardioverter-defibrillator (ICD). Pacemaker and ICD labeling currently cautions physicians against the use of MRI, and MRI manufacturers contraindicate MRI for pacemaker and ICD patients. As discussed in our previous editorial, several studies have demonstrated the potential for MRI to be performed in pacemaker and ICD patients without serious clinical consequence. Studies presented by Sommer et al and Nazarian et al in this issue of Circulation offer further promising evidence in this regard. As with previous studies, however, the authors acknowledge a multitude of limitations that prevent broad applicability of the results. Furthermore, one of these studies was not entirely free from concerning outcomes with the potential for serious clinical events. We view these results as consistent with our previous message that, on a case-by-case basis, the diagnostic benefit from MRI outweighs the presumed risks for some pacemaker and ICD patients. However, the FDA remains firm in its belief that those risks have not yet been characterized and mitigated sufficiently to justify the routine use of MRI in those populations. The FDA continues to believe that a more thorough evaluation of concerns related to heating, arrhythmogenesis, and proper device function during and after MRI, as well as validated MR protocols, should be available before approval for labeling that endorses the use of MRI for pacemaker or ICD patients is obtained.

The public comment on this request was divided on this requested change. We note that the American College of Radiology's ACR Guidance Document for Safe MR Practices: 2007 devotes significant discussion to the need to address the possibility of MRI effects on ferromagnetic implants or foreign bodies, and the need for patient protections. The additional materials submitted by the commenters are mixed. Some authors suggest that MRI might be safely accomplished with close supervision in patients who are not pacemaker dependent while other cite deaths despite physician supervision in patients who have undergone the procedure.

Thus we have determined that this request is premature at this time, and we will retain the current contraindications. Should FDA in the future approve a pacemaker or implantable cardioverter-defibrillator device as safe for use in an MRI environment we would expect to receive a request to reconsider this NCD and review such evidence that may be available at that time.

XI. Conclusion

CMS received a request to delete the national noncoverage of blood flow measurement from the Magnetic Resonance Imaging NCD at 220.2 of the NCD Manual and thus permit local Medicare contractor discretion to cover this use under 220.2(D). The requestor points to an apparent contradiction between this noncoverage provision and the national coverage of magnetic resonance imaging under the Magnetic Resonance Angiography NCD at 220.3 of the NCD Manual.

CMS also received a separate request to revise the reference to cardiac pacemakers to permit coverage for MRI when a beneficiary has an implanted device that has been designed, tested and FDA labeled for use in the MRI environment. NCD 220.2 currently includes the following:

The MRI is not covered when the following patient-specific contraindications are present. It is not covered for patients with cardiac pacemakers or with metallic clips on vascular aneurysms.

We have considered both requests in this reconsideration.

CMS finds that the blanket noncoverage of MRI for blood flow determination at 220.2 is no longer supported by the available evidence. Therefore we will remove the phrase "blood flow measurement," from the Nationally Noncovered Indications at 220.2(C)(2) of the National Coverage Determinations Manual. Pursuant to 220.2(D), local Medicare contractors will have discretion to cover (or not cover) this use.

CMS has not found evidence that MRI improves health outcomes in beneficiaries who have an implanted cardioverter-defibrillator or cardiac pacemaker approved by FDA for use in an MRI environment. We also note that there are currently no such devices. Therefore we will not change this provision of the NCD Manual. We will retain the current contraindications.

APPENDIX A

General Methodological Principles of Study Design
(Section VI of the Decision Memorandum)

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention’s potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).
- Co-interventions or provision of care apart from the intervention under evaluation (performance bias).
- Differential assessment of outcome (detection bias).
- Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

Randomized controlled trials
Non-randomized controlled trials
Prospective cohort studies
Retrospective case control studies
Cross-sectional studies
Surveillance studies (e.g., using registries or surveys)
Consecutive case series
Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived. Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

Appendix B: Evidence Summary and Analysis of Original Requester Submitted Evidence								
Lead Author	**Year**	**Type Study**	**N**	**Age ≥65 F = FEW S = Some**	**Compared Modalities Name , N = CMRI only**	**Pathology**	**Outcome Measure(s)**	**MRI Judgment**
Arheden	1999	Series	24	N	CMRI, Radionuclide angiography	MR	Pulmonary-to-systemic blood flow ratio (QP/QS)	CMRI = reference (ref) standard (std)
Beerbaum	2001	Prospective series	50	N Children	CMRI, Oximetry	Atrial- or ventricular-level left-to-right shunt	Blood Flow Rate	CMRI acceptable

Appendix B: Evidence Summary and Analysis of Original Requester Submitted Evidence								
Lead Author	**Year**	**Type Study**	**N**	**Age ≥65 F = FEW S = Some**	**Compared Modalities Name , N = CMRI only**	**Pathology**	**Outcome Measure(s)**	**MRI Judgment**
Caruthers	2003	Retrospective cohort	24	S	CMRI, ECHO	AS	Flow velocity Aortic & left ventricular outflow tract	CMRI reliable
Eichenberger	1993	Series - convenience	19	N	CMRI, ECHO, Cardiac catheterization (CC)	AS	Flow velocity and pressure gradients across AV	CMRI reliable
Fujita	1994	Series - convenience	29	S	CMRI, ECHO	Mitral regurgitation (MR)	Regurgitant volume	CMRI reliable
Gelfand	2006	Series- consecutive	141	S	CMRI, ECHO	Mitral and aortic regurgitation (AR)	Regurgitation severity	CMRI reliable
Heidenreich	1995	Retrospective cohort	16	S	CMRI, ECHO	Mitral Stenosis (MS)	Peak flow velocity across MV	CMRI reliable
Helbing	1996	Series-control	29	N	N	Tetralogy of Fallot	Right ventricular time-volume curve29	CMRI = ref standard
Honda	1993	Series	31	N	CMRI, ECHO	AR	Regurgitant flow	CMRI reliable

Appendix B: Evidence Summary and Analysis of Original Requester Submitted Evidence								
Lead Author	**Year**	**Type Study**	**N**	**Age ≥65 F = FEW S = Some**	**Compared Modalities Name , N = CMRI only**	**Pathology**	**Outcome Measure(s)**	**MRI Judgment**
Hundley	1995	Series	23	F	CMRI, Cardiac catheterization	MR	Cardiac output	CMRI reliable
Hundley-2	1995	Series	23	F	CMRI, Cardiac catheterization	MR	Regurgitation volume LV	CMRI reliable
Kilner	1993	Series- consecutive	16	F	CMRI, ECHO	MS,AS	Peak poststenotic jet velocity	CMRI reliable
Kizilbash	1993	Series	22	F	CMRI, ECHO	MR	Regurgitation volume/fraction LV	CMRI = ref std
Li	2003	Series- consecutive	52	N	CMRI, ECHO	Tetralogy of Fallot	Pulmonary regurgitant fraction (PRF)	CMRI reliable
Lin	2004	Series	17	F	CMRI, ECHO	MS	Mitral valve areas (MVAs)	CMRI reliable
Powell	2003	Prospective series	20	N	MRI, oximetry	Interatrial communication	Qp/Qs	CMRI reliable
Rebergen	1993	Series	18	N	N	Tetralogy of Fallot	Volumetric Flow	CMRI = ref std

Appendix B: Evidence Summary and Analysis of Original Requester Submitted Evidence								
Lead Author	**Year**	**Type Study**	**N**	**Age ≥65 F = FEW S = Some**	**Compared Modalities Name , N = CMRI only**	**Pathology**	**Outcome Measure(s)**	**MRI Judgment**
Tanaka	2007	Series-consecutive	22	Y	N	Aortic Stenosis (AS)	Aortic valve area (AVA)	CMRI = ref std
Westenberg	2005	Series- consecutive for subjects, convenience control	30	F	N	MR	Mitral valve flow	CMRI 3-D = ref std
Yap	2007	Series	20	N	CMRI, ECHO	Stenotic bicuspid aortic valves	Aortic Valve Area	CMRI reliable

Appendix C: Additional Evidence								
Lead Author	**Year**	**Type Study**	**N**	**Age ≥ 65 F = FEW S = Some**	**Compared Modalities Name , N = CMRI only**	**Pathology**	**Relevant Outcome Measure(s)**	**MRI Judgment**
Aaberg	2001	RCT	100	N	CMRI, CT	Refractory Angina	LVEF, LVEDV	CMRI acceptable
Berg	1998	RCT	40	Y	CMRI	Aortic Valve Replacement (AVR)	LVESM	CMRI ref std

Appendix C: Additional Evidence								
Chan	2007	RCT	51	Y	CMRI	Systolic HF patients	LVEF, LVEDVI VESV, LVM	CMRI ref std
Foster	1998	Series	29	F	CMRI	AMI	LVM, LVV	CMRI ref std
Grothues	2002	Series	60	Y	ECHO, CMRI	HF/LVH/Normal	LVV. LVM	CMRI more repeatable than ECHO
Grothues	2004	Series	60	Y	CMRI	HF/LVH/Normal	RVV, RVM, interstudy reproducibility	CMRI ref std
Lim	2005	Series	36	Y	ECHO, CMRI	AMI	LVESV, LVEDV	CMRI more accurate than ECHO
Malm	2005	Series-consecutive	100	F	CMRI	Known or suspected heart disease	LVEF	CMRI = ref std
Nanda	2003	RCT/Series	206/203 (26)	Y	ECHO, CMRI	Range of indications for ECHO	Endocardial border delineation (EBD)	CMRI reliable alternative for wall motion, especially when ECHO not good study
Paelnick	2005	Series	18	Y	ECHO, CMRI	Hypertensive heart disease	LV filling pressure	CMRI is in good agreement with ECHO
White	1988	Series	22	N	ECHO, CMRI	MI	LV contractile dysfunction	CMRI comparable to 2-D ECHO

Appendix C: Additional Evidence								

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Bibliography

Aaberg et al. Effects of Transmyocardial Revascularization on Myocardial Perfusion and Systolic Function Assessed by Nuclear and Magnetic Resonance Imaging Methods. Scand Cardiovasc J. 2001; 35; 8–13.

Arheden H, Holmqvist C, Thilen U et al. Left-to-right cardiac shunts: comparison of measurements obtained with MR velocity mapping and with radionuclide angiography. Radiology. 1999 May;211(2):453-8.

Berg GA et al. A three year experience with the Toronto stentless porcine valve. Ann Thorac Cardiovasc Surg. 1998 Jun;4(3):138-45.

Carr-White GS et al. Right ventricular function after pulmonary autograft replacement of the aortic valve. Circulation. 1999 Nov 9;100(19 Suppl):II36 -41.

Caruthers SD, Lin SJ, Brown P, Watkins MP et al. Practical value of cardiac magnetic resonance imaging for clinical quantification of aortic valve stenosis: comparison with echocardiography. Circulation. 2003 Nov 4 ;108(18):2236-43. Epub 2003 Oct 20.

Dorfman T et al. Cardiac atrophy in women following bed rest. J Appl Physiol. 2007;103: 8–16.

Eichenberger AC, Jenni R, von Schulthess GK. Aortic valve pressure gradients in patients with aortic valve stenosis: quantification with velocity-encoded cine MR imaging. AJR Am J Roentgenol. 1993 May;160(5):971-7.

Faris O, Shein M. Food and Drug Administration Perspective Magnetic Resonance Imaging of Pacemaker and Implantable Cardioverter-Defibrillator Patients. Circulation 2006; 114:1232-1233.

Fujita N, Chazouilleres AF, Hartiala JJ et al. Quantification of mitral regurgitation by velocity-encoded cine nuclear magnetic resonance imaging. J Am Coll Cardiol. 1994 Mar 15 ;23(4):951-8.

Gelfand EV, Hughes S, Hauser TH et al. Severity of mitral and aortic regurgitation as assessed by cardiovascular magnetic resonance: optimizing correlation with Doppler echocardiography. J Cardiovasc Magn Reson. 2006;8(3):503-7.

Gimbel J. Safe, sensible, sagacious: responsible scanning of pacemaker patients. European Heart J. 2005. 26: Online publish-ahead-of-print 9 June 2005.

Grothues F et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol. 2002 Jul 1 ;90(1):29-34.

Grothues F et al. Interstudy reproducibility of right ventricular volumes, function, and mass with cardiovascular magnetic resonance. Am Heart J. 2004 Feb ;147(2):218-23.

Heidenreich PA, Steffens J, Fujita N et al. Evaluation of mitral stenosis with velocity-encoded cine-magnetic resonance imaging. Am J Cardiol. 1995 Feb 15;75(5):365-9.

Honda N, Machida K, Hashimoto M et al. Aortic regurgitation: quantitation with MR imaging velocity mapping. Radiology. 1993 Jan;186(1):189-94.

Hundley WG, Li HF, Hillis LD, Meshack BM et al. Quantitation of cardiac output with velocity-encoded, phase-difference magnetic resonance imaging. Am J Cardiol. 1995 Jun 15 ;75(17):1250-5.

Hundley WG, Li HF, Willard JE, Landau C, et al. Magnetic resonance imaging assessment of the severity of mitral regurgitation. Comparison with invasive techniques. Circulation. 1995 Sep 1 ;92(5):1151-8.

Jelinek, JS et al. "Diagnosis of Primary Bone Tumors with Image-Guided Percutaneous Biopsy: Experience with 110 Tumors." *Radiology*. 223 (2002): 731 - 737.

Kanal E, Barkovich A, Bell C et al. for the ACR Blue Ribbon Panel on MR Safety. ACR Guidance Document for Safe MR Practices: 2007. AJR. 2007 Jun; 188:1447-1474.

Kilner PJ, Manzara CC, Mohiaddin RH et al. Magnetic resonance jet velocity mapping in mitral and aortic valve stenosis. Circulation. 1993 Apr;87(4):1239-48.

Kizilbash AM, Hundley WG, Willett DL, Franco F, Peshock RM, Grayburn PA. Comparison of quantitative Doppler with magnetic resonance imaging for assessment of the severity of mitral regurgitation. Am J Cardiol. 1998 Mar 15;81(6):792-5.

Levine GN, Gomes AS, Arai AE, Bluemke DA et al. Safety of magnetic resonance imaging in patients with cardiovascular devices: an American Heart Association scientific statement from the Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology, and the Council on Cardiovascular Radiology and Intervention: endorsed by the American College of Cardiology Foundation, the North American Society for Cardiac Imaging, and the Society for Cardiovascular Magnetic Resonance. Circulation. 2007 Dec 11;116(24):2878-91. Epub 2007 Nov 19.

Li W, Davlouros PA, Kilner PJ et al. Doppler-echocardiographic assessment of pulmonary regurgitation in adults with repaired tetralogy of Fallot: comparison with cardiovascular magnetic resonance imaging. Am Heart J. 2004 Jan;147(1):165-72.

Lim TK, Burden L, Janardhanan R, et al. Improved accuracy of low-power contrast echocardiography for the assessment of left ventricular remodeling compared with unenhanced harmonic echocardiography after acute myocardial infarction: comparison with cardiovascular magnetic resonance imaging. J Am Soc Echocardiogr 2005;18:1203-1207.

Lin SJ, Brown PA, Watkins MP et al. Quantification of stenotic mitral valve area with magnetic resonance imaging and comparison with Doppler ultrasound. J Am Coll Cardiol. 2004 Jul 7 ;44(1):133-7.

Malm S, Sagberg E, Larsson H, Skjaerpe T. Choosing apical long-axis instead of two-chamber view gives more accurate biplane echocardiographic measurements of left ventricular ejection fraction: a comparison with magnetic resonance imaging. J Am Soc Echocardiogr. 2005 Oct;18(10):1044-50.

Nanda NC, Kitzman DW, Dittrich HC, Hall G; Imagent Clinical Investigators Group. Imagent improves endocardial border delineation, inter-reader agreement, and the accuracy of segmental wall motion assessment. Echocardiography. 2003 Feb;20(2):151-61.

Paelinck BP, de Roos A, Bax JJ Feasibility of tissue magnetic resonance imaging: a pilot study in comparison with tissue Doppler imaging and invasive measurement. J Am Coll Cardiol. 2005 Apr 5;45(7):1109-16.

Perrier, et. al. Multidetector-Row Computed Tomography in Suspected Pulmonary Embolism, New England Journal of Medicine, 2005; 352(17); 1760-1768, Powell AJ, Tsai-Goodman B, Prakash A, Greil GF, Geva T. Comparison between phase-velocity cine magnetic resonance imaging and invasive oximetry for quantification of atrial shunts. Am J Cardiol. 2003 Jun 15;91(12):1523-5, A9.

Sommer T, Naehle, CP, Yang A et al. Strategy for Safe Performance of Extrathoracic Magnetic Resonance Imaging at 1.5 Tesla in the Presence of Cardiac Pacemakers in Non–Pacemaker-Dependent Patients A Prospective Study With 115 Examinations. Circulation. 2006;114: 1285-1292.

Tanaka K, Makaryus AN, Wolff SD. Correlation of aortic valve area obtained by the velocity-encoded phase contrast continuity method to direct planimetry using cardiovascular magnetic resonance. J Cardiovasc Magn Reson. 2007;9(5):799-805.

Westenberg JJ, Doornbos J, Versteegh MI et al. Accurate quantitation of regurgitant volume with MRI in patients selected for mitral valve repair. Eur J Cardiothorac Surg. 2005 Mar ;27(3):462-6; discussion 467. Epub 2004 Dec 19.

White RD, Cassidy MM, Cheitlin MD et al. Segmental evaluation of left ventricular wall motion after myocardial infarction: magnetic resonance imaging versus echocardiography. Am Heart J. 1988 Jan;115(1 Pt 1):166-7/.5.

Yap SC, van Geuns RJ, Meijboom FJ et al. A simplified continuity equation approach to the quantification of stenotic bicuspid aortic valves using velocity-encoded cardiovascular magnetic resonance. J Cardiovasc Magn Reson. 2007;9(6):899-906.

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